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60/463,933 18 April 2003 (18.04.2003) US
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(54) Title: HIGH THROUGHPUT FUNCTIONAL GENOMIC SCREENING METHODS FOR OSTEOARTHRITIS

(57) Abstract: High-throughput functional screening assays are provided that identify genes and gene products that are associated with the pathogenesis of osteoarthritis (OA) in chondrocytes. In addition, genes and gene products identified by such functional assays are also provided. The genes and gene products provided herein are useful *inter alia* for diagnosing OA in individuals and as drug targets for identifying drugs to treat OA.

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP2004/004055

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, COMPENDEX, EMBASE, MEDLINE, PAJ, WPI Data, INSPEC

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 02/070737 A (ZHANG HONGWEI ; CHONDROGENE INC (CA); LIEW CHOONG-CHIN (CA); MARSHALL) 12 September 2002 (2002-09-12) claims 1-57; examples 4,10	1-14, 16-20
X	WO 94/11532 A (UNIV JEFFERSON ; PROCKOP DARWIN J (US); ALA KOKKO LEENA (US); WILLIAMS) 26 May 1994 (1994-05-26) abstract; claims 1-18	1-14, 16-20
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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *G* document member of the same patent family

Date of the actual completion of the international search

30 December 2004

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29.03.05

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP2004/004055

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>ABBASZADE I ET AL: "Cloning and characterization of ADAMTS11, an aggrecanase from the ADAMTS family" JOURNAL OF BIOLOGICAL CHEMISTRY, AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, BALTIMORE, MD, US, vol. 274, no. 33, 13 August 1999 (1999-08-13), pages 23443-23450, XP002238291 ISSN: 0021-9258 page 23443, columns 1-2</p>	1-14, 16-20
A	<p>US 5 558 988 A (PROCKOP DARWIN J ET AL) 24 September 1996 (1996-09-24) the whole document</p>	1-14, 16-20

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2004/004055

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-14, 16-20 (all partly)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-14, 16-20 (all partly)

Methods for identifying nucleic acids associated with osteoarthritis employing as a marker aggrecanase or aggrecan.

2. claims: 1-14, 16-20 (all partly)

Methods for identifying nucleic acids associated with osteoarthritis employing as a marker MMP-13.

3. claims: 1-14, 16-20 (all partly)

Methods for identifying nucleic acids associated with osteoarthritis employing as a marker collagen.

4. claims: 1-14, 16-20 (all partly)

Methods for identifying nucleic acids associated with osteoarthritis employing as a marker iNOS.

5. claims: 1-14, 16-20 (all partly)

Methods for identifying nucleic acids associated with osteoarthritis employing as a marker Cox-2.

6. claims: 1-14, 16-20 (all partly)

Methods for identifying nucleic acids associated with osteoarthritis employing as a marker decorin.

7. claims: 1-13, 15-20 (all partly)

Methods for identifying nucleic acids associated with osteoarthritis employing as a marker C17.

8. claims: 1-13, 15-20 (all partly)

Methods for identifying nucleic acids associated with osteoarthritis employing as a marker SMOC2.

9. claims: 1-13, 15-20 (all partly)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Methods for identifying nucleic acids associated with osteoarthritis employing as a marker OSF-2.

10. claims: 1-13, 15-20 (all partly)

Methods for identifying nucleic acids associated with osteoarthritis employing as a marker MARCKS.

11. claims: 1-13, 15-20 (all partly)

Methods for identifying nucleic acids associated with osteoarthritis employing as a marker retinoic acid receptor beta.

12. claims: 1-13, 15-20 (all partly)

Methods for identifying nucleic acids associated with osteoarthritis employing as a marker Zic1.

13. claims: 1-13, 15-20 (all partly)

Methods for identifying nucleic acids associated with osteoarthritis employing as a marker BASP1.

14. claims: 1-13, 15-20 (all partly)

Methods for identifying nucleic acids associated with osteoarthritis employing as a marker DIM1.

15. claims: 21-26

Methods for identifying nucleic acids associated with osteoarthritis employing a chondrocyte proliferation assay.

16. claims: 27-40 (all partly)

Methods for identifying individuals having osteoarthritis or compounds to treat the latter comprising a candidate gene from Table V.

17. claims: 27-40 (all partly)

Methods for identifying individuals having osteoarthritis or compounds to treat the latter comprising a candidate gene from Table VI.

FURTHER INFORMATION CONTINUED FROM PCT/SA/ 210

18. claims: 41-45 (all partly)

Pharmaceutical compositions comprising modulators of genes disclosed in Table V.

19. claims: 41-45 (all partly)

Pharmaceutical compositions comprising modulators of genes disclosed in Table VI.

20. claims: 46-47 (all partly)

Methods to treat, prevent, or amelioarte osteoarthritis comprising genes from the group disclosed in Table V.

21. claims: 46-47 (all partly)

Methods to treat, prevent, or amelioarte osteoarthritis comprising genes from the group disclosed in Table VI.

22. claim: 48

Diagnostic kit for detection of mRNA or protein levels comprising candidate gene from table V.

23. claim: 48

Diagnostic kit for detection of mRNA or protein levels comprising candidate gene from table VI.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

P01/EP2004/004055

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 02070737	A	12-09-2002	AU 2002237124 A2	19-09-2002
			BR 0207657 A	26-10-2004
			WO 02070737 A2	12-09-2002
			CA 2439504 A1	12-09-2002
			EP 1404868 A2	07-04-2004
			JP 2004536575 T	09-12-2004
			US 2004037841 A1	26-02-2004
			US 2004013663 A1	22-01-2004
			US 2004248169 A1	09-12-2004
WO 9411532	A	26-05-1994	US 5558988 A	24-09-1996
			WO 9411532 A1	26-05-1994
			US 5948611 A	07-09-1999
US 5558988	A	24-09-1996	WO 9411532 A1	26-05-1994
			US 5948611 A	07-09-1999